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		Art Unit	1849
		Examiner Name	Kimberly A. Ballard
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Attorney Docket No.: 15270J-004743US
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

In re application of:

DALE B. SCHENK

Application No.: 09/724,319

Filed: November 27, 2000

For: PREVENTION AND TREATMENT OF
AMYLOIDOGENIC DISEASE

Examiner: Kimberly A. Ballard

Art Unit: 1649

AMENDED APPELLANT'S BRIEF
UNDER 37 C.F.R. § 41.37 (c)(1)(iii)

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Notification of Non-Compliant Appeal Brief dated December 28, 2006, submitted herewith is an amended appeal brief that includes a statement of the status of all claims and identifies claims on appeal.

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1. REAL PARTY IN INTEREST

Elan Pharma International Ltd.

2. RELATED APPEALS AND INTERFERENCES

An Appeal is pending in related US Application No. 09/723,765.

3. STATUS OF CLAIMS

Claims 56-58, 61, 63-66, 71-79, 81, 85, 86, 92-94, 97, 99, 164-191, 194-205, and 207-209 are rejected and appealed. Claims 1-55, 59, 60, 62, 67-70, 80, 82, 84, 87-91, 95, 96, 98, 100, 192, 193, and 206 are cancelled. Claims 83 and 101-163 are withdrawn. Appellant has requested cancellation of claims 83 and 101-163 by an amendment after final filed October 10, 2006 but has not yet heard whether this amendment will be entered.

4. STATUS OF AMENDMENTS

The amendment after final submitted October 10, 2006 requested cancellation of claims 83 and 101-163 and requested correction of typographic errors in claims 93, 94, 166 and 197. None of these amendments affects the merits. The listing of claims in the Claims Appendix assumes the amendment will be entered.

5. SUMMARY OF CLAIMED SUBJECT MATTER

There are three independent claims pending in this appeal: Claims 56, 97 and 183.

Claim 56 is directed to a method of treating a patient having Alzheimer's disease. The method comprises administering to the patient an effective dosage of pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of the beta-amyloid peptide (hereinafter A β) and a pharmaceutical carrier. Methods of treatment of Alzheimer's disease using such antibodies are described in the specification at e.g., p. 10, lines 1-15, and lines 30-33, and p. 14, lines 14-24. The effectiveness

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of antibodies binding to a 13-28 epitope is described in the specification at *e.g.*, p. 78, lines 16-10. The use of human, humanized and chimeric antibodies is described in the specification at *e.g.*, p. 16, line 25 to p. 23, line 15. The methods are illustrated particularly by Example X1 at pp. 70-78 of the specification. This example shows that antibody designated 266, which binds to a 13-28 epitope of A β , when administered to a transgenic mouse model of Alzheimer's disease results in a statistically significant reduction in the level of A β (the presumed pathogenic agent of Alzheimer's disease) in the cerebellum of such mice.

Claim 97 is directed to a pharmaceutical composition comprising a human or humanized antibody which specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier. Pharmaceutical compositions are described in the specification at *e.g.*, p.31, line 18 to p. 33, line 11.

Claim 183 parallels claim 56, except that claim 183 recites a method of reducing risk or delaying onset of Alzheimer's disease in a patient at risk of the disease. The method , comprises administering to the patient an effective dosage of a pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier and thereby reduce the risk or delay the onset of the disease in the patient. Methods of reducing risk or delaying onset are described in the specification at *e.g.*, p. 27, lines 12-14.

6. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

6.1 Whether claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205, and 207-209 should be rejected for obviousness-type double patenting over claims 43-44, 134-135, 138-139, 142-145, 146, 148 and 154-157 of US Application No. 09/979,701.

6.2 Whether claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205 and 207-209 lack written description under 35 U.S.C. § 112, first paragraph.

6.3 Whether claims 56-58, 61, 63-66, 71-79, 81 and 85-86, 92-94, 183-191, 194-205, and 207-209 lack enablement under 35 U.S.C. § 112, first paragraph

6.4. Whether claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-204 and 207-209 would have been obvious under 35 USC 103(a) over Schenk *et al.*, US 5,593,846 in view of Queen US 5,530,101.

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7. ARGUMENT

7.1. Obviousness-Type Double Patenting

US Application No. 09/979,701 was expressly abandoned on July 13, 2006, so the rejection for provisional obviousness-type double patenting over this application is moot.

7.2. The Claims Do Not Lack Written Description Under 35 U.S.C. § 112, First Paragraph

The rejection is based on the allegation that applicants have amended the claims to recite a "human antibody 266" that binds to the epitope 13-28 of A β when the specification and prior art recognize mAb 266 as a mouse monoclonal. The Examiner further alleges that the specification does not disclose a human antibody 266 (final office action, paragraph bridging pp. 4-5).

In reply, the rejection does not accurately reflect the claim language. None of the claims specifies a human 266 antibody. Claims 56, 97 and 183 do specify a human antibody that binds to an epitope within residues 13-28 of A β , but do not refer to a human 266 antibody. The 266 antibody is a mouse antibody binding to an epitope within residues 13-28 of A β , as described in Example XI of the specification. Support for human antibodies with the same epitope as mouse antibodies described in Example XI of the specification is provided at e.g., p. 18, lines 8-10. Because the rejection is not based on the actual claim language, and the actual claim language is supported by the specification, it is respectfully submitted that the rejection should be reversed.

7.3. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 183-191, 194-205 and 207-209 Do Not Lack Enablement Under 35 U.S.C. § 112, First Paragraph

The principal issue raised by the rejection is whether a claim to a method of treating Alzheimer's disease or delaying or reducing risk of onset of Alzheimer's disease can be enabled without evidence to show that the method can achieve a *complete* cure or *complete*

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prevention of disease. The Examiner acknowledges that the claimed methods are enabling for reducing amyloid burden in an animal model of Alzheimer's disease (final office action at p. 5, second paragraph, paragraph bridging pp. 6-7) and that the use of antibodies specific for an epitope comprising residues 13-28 of A β is feasible for treating Alzheimer's disease (final office action at p. 7, second paragraph). However, the Examiner alleges lack of enablement on the grounds that the Appellant has not shown the claimed methods can achieve a complete cure or complete prevention (final office action at p. 5, paragraph).

The Examiner's assertion that treatment and reducing risk or delaying onset of disease are synonymous with cure and prevention of disease (final office action at p. 5, second paragraph) is incorrect. Treatment of a disease includes but does not require completely curing a disease. Similarly, delaying or reducing risk of onset of a disease includes but does not require completely preventing a disease (*see, e.g.*, specification at p. 27, lines 12-20). As properly construed, Appellant respectfully submits that the claims are enabled.

Enabling the full scope of a claim does not necessarily require enabling every embodiment within the claim. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1576, 224 USPQ 409, 414 (Fed. Cir. 1984). This principle is applied to a method of treatment by *In re Cortright*, 165 F.3d 1353, 49 USPQ2d 1464 (Fed. Cir. 1999). One of the claims at issue in *In re Cortright* was directed to a method of treating baldness. The Board had rejected the claim for lack of enablement on the basis that the specification did not show restoring the user's hair to its original state (*i.e.*, a full head of hair) but only some improved growth characterized as "filling-in some" or "fuzz" (*Id.* at 1358, 49 USPQ2d at 1467). The Federal Circuit construed the claims as meaning that the claimed method increased the amount of hair grown on the scalp but did not necessarily produce a full head of hair (*Id.* at 1359, USPQ2d at 1468). The Federal Circuit concluded that the claims, so construed, were enabled, notwithstanding the lack of evidence that complete restoration could be achieved.

The same principle is illustrated in a different technology by *CFMT, Inc. v. Yieldup Int'l Corp.*, 349 F.3d 1333, 1338, 68 USPQ2d 1940, 1944 (Fed. Cir. 2003). The patent at issue was directed to a method of cleaning semi-conductor wafers. The available evidence showed that the disclosed method could remove some contaminants, but could not remove all contaminants, nor even achieve removal of contaminants to a commercial standard. The Federal Circuit reversed the district court's holding of lack of enablement.

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In essence the district court set the enablement bar too high. Enablement does not require an inventor to meet lofty standards for success in the commercial marketplace. Title 35 does not require that a patent disclosure enable one of ordinary skill in the art to make and use a perfected commercially viable embodiment absent a claim limitation to that effect.

In sum, any meaningful "cleaning" would satisfy the claimed goal of "cleaning of semiconductor wafers."

Id. at . 1338-1340, 68 USPQ2d at 1944-45.

A recent unpublished decision of the USPTO Board of Patent Appeals and Interferences is instructive in applying the above Federal Circuit precedents to claims encompassing methods of treatment. *Ex parte Saito*, Appeal No. 2005-1442 (BPAI 2005, nonprecedential opinion) concerned claims directed to methods of introducing a nucleic acid into a subject by transplanting a hair follicle modified to contain the nucleic acid. The claims were rejected by the Examiner for lack of enablement because, although the claims were not limited to therapeutic methods, the claims encompassed such methods, and the Examiner took the view that undue experimentation would be required to achieve therapeutic levels of gene expression. The Board followed the precedent of *In re Corthright* in reversing the Examiner.

As with the present claims, the claims in *Corthright* encompassed a method of obtaining results that might be difficult to achieve: here, therapeutically effective gene therapy; in *Corthright*, complete restoration of hair growth. However, as in *Corthright*, the present claims do not require that particular result: the present claims require only introducing or delivering a nucleic acid; *Corthright's* claims required only some restoration of hair growth.

The court in *Corthright* did not dispute the board's conclusion that completely restoring hair growth using Bag Balm® would require undue experimentation [citation omitted]. The court nonetheless concluded that the claimed method was not nonenabled merely because it encompassed one difficult-to-achieve outcome. The same reasoning applies here: the examiner may be correct that achieving clinically useful gene therapy using the claimed method would require undue experimentation, but the claims are not nonenabled merely for encompassing that difficult-to-achieve outcome.

Ex parte Saito, Appeal No. 2005-1442, at pp. 6-7.

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Here, as in *In re Cortright* or *Ex Parte Saito*, the present claims include but do not require a complete cure or complete prevention. Assuming *arguendo* that the claimed methods cannot completely cure or prevent Alzheimer's disease, they would be no different than treatment or prophylaxis with many other highly successful drugs. For example, it is well known that the commercial success of certain cancer drugs is measured in increments of extending the life of a patient by few months, a result far removed from complete cure or prevention. Further, a quick search of the PTO database reveals that the Patent Office has granted thousands of patents to methods of treatment and/or prophylaxis of disease notwithstanding that it is common knowledge that few drugs achieve such lofty goals as complete cure or complete prevention. In these circumstances, Appellant submits that in the presently claimed methods, as in other patents claiming methods of treatment or prophylaxis, the possibility that the methods may not achieve a complete cure or complete prevention is not detrimental to enablement and need not be excluded from the claims.

The Examiner's position is also based in part on alleged inadequacies of the PDAPP mouse model of Alzheimer's disease used in the specification as being representative of Alzheimer's disease in humans (paragraph bridging pp. 6-7). The Examiner alleges that reduction in amyloid burden in such a model is not representative of achieving cognitive effects (final office at p. 9, third paragraph). Appellant submits that the present issues regarding the alleged inadequacy of animal trials are essentially the same as those presented in *In re Brana*, 34 USPQ2d 1436 (Fed. Cir. 1995).

The *Brana* court reversed a rejection under 35 U.S.C. § 112, first paragraph based on the PTO's refusal to accept data from testing compounds in an animal model of cancer (*Id.* at 1444). The animal model at issue in *Brana* was formed by injecting cancer cells into mice. The PTO took the position that the model was not fully representative of human cancers because the mice did not naturally develop cancers (*Id.* at 1440). The PTO argued that "*in vivo* tests in animals are only preclinical tests to determine whether a compound is suitable for processing in the second stage of testing, [meaning] *in vivo* testing in humans, and therefore are not reasonably predictive of the success of the claimed compounds for treating cancer in humans" (*Id.* at 1142).

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The Federal Circuit reversed the rejection as "arbitrary and capricious." The Federal Circuit held that "Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings" (*Id.* at 1442).

Here, there is abundant evidence that the PDAPP animal model used in the Examples of the specification shows many similarities with Alzheimer's disease, and is regarded as being useful for screening drugs. For example, Games *et al.*, *Nature* 373: 523-527 (1995) concludes:

A most notable feature of these transgenic mice is their Alzheimer-like neuropathology . . . Our transgenic model . . . offers a means to test whether compounds that lower A β production and/or reduce its neurotoxicity *in vitro* can produce beneficial effects in an animal model prior to advancing such drugs into human clinical trials.

See p. 527, first column, second paragraph.

Similarly, Chen *et al.*, *Progress in Brain Research*, 17:327-337 (1998) conclude that the PDAPP mouse model, although not displaying all pathological hallmarks of Alzheimer's disease, does "display most of them in a robust manner that increases with age and gene dosage" and provides a "useful model for the testing of various therapeutic interventions directed towards specific aspects of the neurodegenerative process (*see p. 333, first column, last paragraph*).

Moreover, post-filing evidence demonstrates that a treatment resulting in reduced amyloid burden in the PDAPP mouse model does result in cognitive benefits in humans. The present specification shows that active administration of A β 42 results in reduced levels of A β in the brains of PDAPP mice. A subsequent human clinical trial showed statistically significant cognitive benefits in humans (Hock *et al.*, *Neuron* 38, 542-554 (2003)). The clinical trial involved administration of A β rather than administration of an antibody to A β as recited in the present claims. However, the human clinical evidence shows that an agent (*i.e.*, A β 42) having pharmacological activity in reducing or eliminating plaque burden in the PDAPP mouse model also has useful clinical activity in the human trial. Given this correlation, and the art-recognized

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similarities in pathology between the PDAPP mouse and human disease, it is all the more likely that other agents having pharmacological activity in the PDAPP mouse, such as the antibodies claimed in the instant application, also confer clinically useful benefits in humans.

That the PDAPP mouse model does not mimic the human disease in every respect was also true of the mouse model in *Brana* and probably every other mouse model of human disease. As *Brana* made clear, rejection of data from a mouse model for this reason is arbitrary and capricious.

The Examiner cites Spooner, *Vaccine* 21, 290-297 (2002) as discussing various issues arising from administration of A β to generate antibodies, including possible (but not demonstrated) autoimmune side effects and variability in production of antibodies. Although the demonstration of cognitive benefits from administration of A β discussed above is relevant in validating the PDAPP mouse model, the issues discussed in Spooner are not relevant to the claimed methods. Autoimmune side effects from immunization with A β or variability in antibody production from such immunization are not expected to be of concern when no immunization with A β is performed.

The Examiner alleges that Walker, *J. Neuropath. Exp. Neurol.* 53, 377-383 (1994) administered a 10D5 antibody to monkeys without apparent reduction of amyloid burden. However, Walker was simply trying to label amyloid for purposes of detection and did not contemplate therapeutic treatment. By contrast, the present application provides data showing that an appropriate regime of 10D5 intended for therapeutic treatment does in fact reduce levels of A β in the brain of a transgenic mouse model of Alzheimer's disease (see Example XI). Moreover, the 10D5 antibody is not disclosed by Walker (or elsewhere) as binding to the claimed 13-28 epitope of A β .

The Examiner cites Goldsby, *Immunology* 4th Ed, Ch. 18 (2002) as discussing the immunogenicity of mouse antibodies. However, the present claims specify human, humanized or chimeric antibodies. As the Examiner has herself noted in connection with the rejection under 35 USC 103, such antibodies have reduced immunogenicity relative to mouse antibodies. Because reduced immunogenicity allows repeated administration of human, humanized or chimeric antibodies, the Examiner's argument regarding alleged lack of formation of

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immunological memory from passive administration of antibodies is not relevant to the claimed invention.

A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as being in compliance with the enablement requirement of 35 USC 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971). For these reason discussed above, it is respectfully submitted that the Examiner has not provided sufficient basis to doubt that the claims can be practiced without undue experimentation based on the teaching of the specification.

7.4. Claims 56-58, 61, 63-66, 71-79, 81, 85-86, 92-94, 97, 99, 164-191, 194-205 and 207 Would Not Have Been Obvious Over Schenk et al., US 5,593,846 in view of Queen, US 5,530,101

7.4.1 The Examiner's Rationale

The Examiner alleges that the '846 patent discloses the 266 antibody and pharmaceutical compositions containing the same. The Examiner acknowledges that the '846 patent is silent regarding chimeric and humanized antibodies. The Examiner alleges that '101 patent provides discloses humanized and chimeric antibodies in general, and their benefit in reducing immunogenicity.

7.4.2 Summary of the References

The '846 patent discusses detecting A β peptide (also known as β AP) in culture media and body fluids (col. 6, lines 1-15) and screening compounds for capacity to inhibit production of the peptide (cols. 10-11). Such compounds are proposed to be useful for treating Alzheimer's disease (col. 11, lines 15-40). Examples of such compounds are listed at col. 11, lines 5-8. The listed compounds are "small molecules, biological polymers, such as polypeptides, polysaccharides, polynucleotides, and the like." There is no mention of antibodies, particularly not antibodies to A β , as inhibitors of A β production. The 266 antibody and other antibodies to A β are mentioned in the context of assays for detection of A β peptide (see cols. 8

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and 9, and particularly col. 14, lines 13-27). Antibodies binding to the 13-28 epitope are preferred for detection because they can distinguish A β from other fragments.

Conveniently, immunological detection techniques may be employed using binding substances, specific for β AP, such as antibodies, antibody fragments, recombinant antibodies, and the like, which bind with specificity and sensitivity to β AP. In particular, it has been found that antibodies which are monospecific for the junction region of β AP are capable of distinguishing β AP from other APP fragments. The junction region of β AP is centered at amino acids residues 16 and 17, typically spanning amino acids residues 13-28, and such junction-specific antibodies may be prepared using synthetic peptides having that sequence as an immunogen. Particularly suitable detection techniques include ELISA, Western blotting, radioimmunoassay, and the like.

Col. 8, lines 19-36.

Antibody 266 is provided for use in an ELISA binding assay as described at col. 14, lines 14-27. This antibody is provided in a buffer at a nonphysiological pH of 8.3 containing the well known toxic compound, sodium azide (NaN₃).

The excerpts of the '846 patent quoted by the Examiner at p. 13 of the final office action are referring to pharmaceutical compositions of compounds identified by the "screening methods for the identification of β AP production" (first excerpt quoted by Examiner at p. 12 of final office action) disclosed in the patent, not pharmaceutical compositions of the 266 antibody or chimeric or humanized forms thereof. There is no mention of an antibody in any of these excerpts. Antibodies are not relevant to the pharmaceutical compositions described in these excerpts except as a tool to identify the compounds to be included in these pharmaceutical compositions.

The '101 patent discusses general procedures for humanizing antibodies, and the advantages of humanization in reducing immunogenicity, and does not serve to cure the deficiencies of the '846 patent with respect to the claimed invention.

7.4.3 The Cited Art Distinguished

The prior art references when combined must teach or suggest all of the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Here, the cited art when combined does not teach or suggest all limitations of independent claims 56, 97 and 183

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(and claims depending therefrom). The '846 patent does not disclose methods of treating Alzheimer's disease or reducing risk or delaying onset of the same by administering 266 or any other antibody to A β . As discussed above, 266 and other antibodies to A β are used as a means to detect A β and thereby discover inhibitors of A β production. The '846 patent does not disclose using 266 or other antibodies to A β themselves as means of treating, reducing risk or delaying onset of Alzheimer's disease, as required by claims 56 and 183. The '846 patent also does not disclose the 266 antibody or other antibody to A β as being part of a pharmaceutical composition, as specified in claim 97.

As discussed above, the '846 patent provides the 266 antibody for use in an ELISA assay in a buffer of non-physiological pH (8.3) containing a well known toxic compound, sodium azide. Such a toxic laboratory buffer is not a pharmaceutical composition as this term is reasonably understood. As discussed above, all references to methods of treatment, prophylaxis and pharmaceutical compositions in the '846 patent are with respect to inhibitors of A β production and not to antibody 266 or any other antibody to A β . The other reference relied upon by the Examiner, the '101 patent, provides no information regarding treatment of Alzheimer's disease, and thus does nothing to cure the lack of teaching of the '846 patent with respect to use of antibodies to A β in methods of treating or reducing risk or delaying onset of Alzheimer's disease, or inclusion of such antibodies in a pharmaceutical composition.

Furthermore, "[o]bviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *In re Geiger*, 2 USPQ2d 1276 (Fed. Cir. 1987). The motivation must have sufficient "force" to "impel persons skilled in the art to do what applicant has done." *Ex parte Levengood*, 28 USPQ2d 1300, 1302 (BPAI 1993). Here, the asserted benefit of reduced immunogenicity would not have been motivated a skilled person to combine the teaching of the '846 and '101 patents to arrive at human, humanized or chimeric antibodies as specified in the present claims. Reduced immunogenicity is a benefit from therapeutic administration of an antibody to a patient because the patient is less likely to experience side effects from repeated administration of the antibody. However, reduced immunogenicity is irrelevant to ELISA and other conventional immunoassays for which antibodies are used in the '846 patent. Such assays are performed *in vitro* and the antibody never comes into contact with an immune system. As noted above, the '846 patent does not discuss therapeutic administration of 266 or other A β

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antibodies. Without any teaching of a therapeutic benefit, the skilled person would not have been impelled to apply the '101 patent's teaching of humanization on 266 or other antibody discussed in the '846 patent.

Several dependent claims are nonobvious based on additional grounds. Claims 57, 99, and 184 specify a humanized version of antibody 266 deposited as ATCC PTA-6123. Production of a humanized antibody requires knowledge of or ability to determine the sequences of the variable regions of the 266 antibody (see '101 patent). Although the '846 patent refers to the 266 antibody, it does not reference a hybridoma deposit or provide the sequences of the variable regions of the antibody. Without this information, a skilled person would not have been able without undue experimentation to reproduce the 266 antibody, determine the sequences of its variable regions or produce a humanized version thereof.

Claim 92 specifies methods of treating Alzheimer's disease in which a pharmaceutical composition is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously. Claim 207 is directed to an analogous methods of reducing risk or inhibiting onset of the disease. All of these methods administer the pharmaceutical composition at a site in the body separated by the blood brain barrier from the site of the pathology within the brain. As discussed by Walker, *J. Neuropath. Exp. Neurol.* 53, 377-383 (1994), *supra*, conventional wisdom before the priority date of the invention was that antibodies were not expected to cross the blood brain barrier (the "blood-brain barrier prevents the passage of many types of molecules from the bloodstream to the brain . . . rendering vascular delivery of ligands to A β problematic," at p. 377, first column, first paragraph). The present application shows that peripherally administered antibodies (including the 266) antibody are nevertheless effective in reducing levels of A β in the brain. This surprising result further evidences the patentability of claims 92 and 207.

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8. CONCLUSION

For these reasons, it is respectfully submitted that the Board should reverse the rejections.

It is also respectfully submitted that Appellant has provided a statement of the status of all claims and identifies claims on appeal as required under 37 C.F.R. § 41.37 (c)(1)(iii).

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9. CLAIM APPENDIX

56. A method of treating a patient having Alzheimer's disease, comprising administering to the patient an effective dosage of a pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier, and thereby treat the disease in the patient.

57. The method of claim 56, wherein the humanized antibody is a humanized version of the monoclonal antibody (ATCC accession number PTA-6123) for binding to A β .

58. The method of claim 56, wherein the antibody competes with the monoclonal antibody designated as 266 (ATCC accession number PTA-6123) for binding to A β .

61. The method of claim 56, wherein the patient is a human.

63. The method of claim 56, wherein the patient is under 50.

64. The method of claim 56, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.

65. The method of claim 56, wherein the patient has no known risk factors for Alzheimer's disease.

66. The method of claim 56, wherein the antibody is a fragment of an intact antibody that competes with the intact antibody for specific binding to A β , and the antibody fragment is selected from the group consisting of Fab, Fab', F(ab')₂, Fabc, and Fv.

71. The method of claim 56, wherein the antibody is a humanized antibody.

72. The method of claim 71, wherein the humanized antibody is an antibody fragment.

73. The method of claim 66, wherein the antibody is a humanized antibody.

74. The method of claim 56, wherein the antibody is a chimeric antibody.

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75. The method of claim 74, wherein the chimeric antibody is an antibody fragment.
76. The method of claim 66, wherein the antibody is a chimeric antibody.
77. The method of claim 56, wherein the antibody is a bispecific antibody.
78. The method of claim 77, wherein the bispecific antibody is an antibody fragment.
79. The method of claim 66, wherein the antibody is a bispecific antibody.
81. The method of claim 56, wherein the antibody is a polyclonal antibody.
85. The method of claim 56, wherein the isotype of the antibody is IgG1.
86. The method of claim 56, wherein a chain of the antibody is fused to a heterologous polypeptide.
92. The method of claim 56, wherein the pharmaceutical composition is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.
93. The method of claim 56, wherein the pharmaceutical composition is administered in multiple dosages over a period of at least six months.
94. The method of claim 56, wherein the pharmaceutical composition is administered as a sustained release composition.
97. A pharmaceutical composition comprising a human or humanized antibody which specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier.
99. The pharmaceutical composition of claim 97, wherein the humanized antibody is a humanized version of the monoclonal antibody 266 (ATCC accession number PTA-6123).

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164. The pharmaceutical composition of claim 97, which is a sustained release composition.

165. The pharmaceutical composition of claim 97, further comprising a physiologically acceptable diluent.

166. The pharmaceutical composition of claim 165 wherein the diluent is selected from the group consisting of distilled water, physiological phosphate-buffered saline, Ringer's solution, dextrose solution, and Hank's solution.

167. The pharmaceutical composition of claim 166, wherein the diluent is physiological phosphate-buffered saline.

168. The pharmaceutical composition of claim 166, wherein the diluent is dextrose solution.

169. The pharmaceutical composition of claim 97, further comprising a macromolecule.

170. The pharmaceutical composition of claim 169, wherein the macromolecule is selected from the group consisting of proteins, polysaccharides, polylactic acids, polyglycolic acids, copolymers, polymeric amino acids, amino acid copolymers, and lipid aggregates.

171. The pharmaceutical composition of claim 97, wherein the composition is suitable for parenteral administration.

172. The pharmaceutical composition of claim 97, wherein the carrier is a liquid carrier.

173. The pharmaceutical composition of claim 172, wherein the liquid carrier is selected from the group consisting of water, oil, saline, glycerol, and ethanol.

174. The pharmaceutical composition of claim 172, wherein the liquid carrier is propylene glycol.

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175. The pharmaceutical composition of claim 172, wherein the liquid carrier is polyethylene glycol.

176. The pharmaceutical composition of claim 97, further comprising a wetting agent.

177. The pharmaceutical composition of claim 97, further comprising an emulsifying agent.

178. The pharmaceutical composition of claim 97, further comprising a surfactant.

179. The pharmaceutical composition of claim 97, further comprising a pH buffering substance.

180. The pharmaceutical composition of claim 97, wherein the pharmaceutical composition is a liquid solution.

181. The pharmaceutical composition of claim 97, wherein the pharmaceutical composition is a suspension.

182. The pharmaceutical composition of claim 97, which is a solid form suitable for solution in a liquid vehicle.

183. A method of reducing risk or delaying onset of Alzheimer's disease in a patient at risk of the disease, comprising administering to the patient an effective dosage of a pharmaceutical composition comprising a human, chimeric or humanized antibody that specifically binds to an epitope within residues 13-28 of A β and a pharmaceutical carrier and thereby reduce the risk or delay the onset of the disease in the patient.

184. The method of claim 183, wherein the humanized antibody is a humanized version of the monoclonal antibody 266 (ATCC accession number PTA-6123).

185. The method of claim 183, wherein the antibody competes with the monoclonal antibody designated as 266 (ATCC accession number PTA-6123) for binding to A β .

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186. The method of claim 183, wherein the patient is a human.
187. The method of claim 183, wherein the patient is asymptomatic.
188. The method of claim 183, wherein the patient is under 50.
189. The method of claim 183, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.
190. The method of claim 183, wherein the patient has no known risk factors for Alzheimer's disease.
191. The method of claim 183, wherein the antibody is a fragment of an intact antibody that competes with the intact antibody for specific binding to A β , and the antibody fragment is selected from the group consisting of Fab, Fab', F(ab'), Fabc, and Fv.
194. The method of claim 183, wherein the antibody is a humanized antibody.
195. The method of claim 183, wherein the humanized antibody is an antibody fragment.
196. The method of claim 191, wherein the antibody is a humanized antibody.
197. The method of claim 183, wherein the antibody is a chimeric antibody.
198. The method of claim 197, wherein the chimeric antibody is an antibody fragment.
199. The method of claim 191, wherein the antibody is a chimeric antibody.
200. The method of claim 183, wherein the antibody is a bispecific antibody.
201. The method of claim 200, wherein the bispecific antibody is an antibody fragment.
202. The method of claim 191, wherein the antibody is a bispecific antibody.

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203. The method of claim 183, wherein the antibody is a polyclonal antibody.

204. The method of claim 183, wherein the isotype of the antibody is IgG1.

205. The method of claim 183, wherein a chain of the antibody is fused to a heterologous polypeptide.

207. The method of claim 183, wherein the pharmaceutical composition is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.

208. The method of claim 183, wherein the pharmaceutical composition is administered in multiple dosages over a period of at least six months.

209. The method of claim 183, wherein the pharmaceutical composition is administered as a sustained release composition.

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10. EVIDENCE APPENDIX

HOCK *et al.*, "Antibodies against β -Amyloid Slow Cognitive Decline in Alzheimer's Disease," Neuron, 38:542-554 (2003), IDS cite no. 534, submitted April 29, 2005.

GAMES *et al.*, "Alzheimer-type neuropathology in transgenic mice over expressing V717F β -amyloid precursor protein," Nature, 373(6514):523-527 (1995), IDS cite no. 109, submitted August 20, 2001.

CHEN *et al.*, "Neurodegenerative Alzheimer-like pathology in PDAPP 717V \rightarrow F transgenic mice," Progress in Brain Research, 117:327-337 (1998), IDS cite no. 332, submitted April 27, 2004.

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11. RELATED PROCEEDINGS APPENDIX

An Appeal has been filed in related US Application No. 09/723,765. No Board or court decisions have issued at this time.

An Appeal was filed in related US Application No. 09/322,289. A non-final rejection mailed November 17, 2006 reopened prosecution of US Application No. 09/322,289.